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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,898	09/19/2003	Andrew H. Segal	11111/2003	9080

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
06/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,898	SEGAL ET AL.	
	Examiner	Art Unit	
	EMILY M. LE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/04/07 and 12/10/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *28-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 67-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. To allow the entry of the rejection(s) set forth herein, this office action is non-final.

Status of Claims

2. Claims 1-69 are pending. Claims 28-66 are withdrawn for being directed to a non elected invention. Claims 1-27 and 67-69 are under examination.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-27 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babai et al.[1] in view of Faulkner et al.,[2] as evidenced by Masuda et al.[3]

The claims are directed to a composition comprising a nucleic acid molecule encoding a fusion polypeptide comprising i) a first amino acid sequence that can bind to a carbohydrate on a glycoprotein, wherein the carbohydrate is a sialic acid; and ii) a second amino acid sequence comprising the sequence of a ligand for a cell surface polypeptide, wherein the ligand is a ligand for a cytokine receptor. Claims 2-3, which depend on claim 1, require the first amino acid sequence to be N-terminal and C-

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[1] Babai et al. A novel liposomal influenza vaccine (INFLUSOME-VAC) containing hemagglutinin–neuraminidase and IL-2 or GM-CSF induces protective anti-neuraminidase antibodies cross-reacting with a wide spectrum of influenza A viral strains. Vaccine, Volume 20, Issues 3-4, 12 November 2001, Pages 505-515

[2] Faulkner et al. Influenza hemagglutinin peptides fused to interferon gamma and encapsulated in liposomes protects mice against influenza infection. Vaccine, February 14, 2003, Vol. 21, 932-939.

[3] Masuda et al. Substitution of amino acid residue in influenza A virus hemagglutinin affects recognition of sialyl-oligosaccharides containing N-glycolylneuraminic acid. FEBS Letters, 1999, Vol. 464, 71-74.

terminal to the second amino acid sequence, respectively. Claim 4, which depends on claim 1, requires the sialic acid to comprise one of the following structures: N-acetylneuraminic acid, alpha-NeuNAc-[2->6]-Gal, alpha-NeuNAc-[2->6]-GalNAc, alpha-NeuNAc-[2->3]-Gal. Claim 5, which depends on claim 1, requires the first amino acid sequence to comprise a carbohydrate-binding domain of a naturally occurring lectin. Claim 6, which depends on claim 1, requires the first amino acid sequence to comprise at least 10 contiguous amino acids of a hemagglutinin, which is limited to an influenza virus hemagglutinin by claim 7, which is further limited to the HA1 domain of the influenza virus hemagglutinin by claim 8. Claim 9, which depends on claim 7, limits the influenza virus to influenza A virus, which is further limited to an H1 subtype by claim 11, which is further limited to the A/PR/8/34 strain by claim 12. Claim 10, which depends on claim 9, limits the influenza virus to a subtype that infects humans, which is limited to the H2 or H3 subtype by claim 13. Claim 14, which depends on claim 7, requires the virus be of a subtype that does not infect humans. Claim 15, which depends on claim 1, limits the ligand for a cell surface polypeptide to a ligand for a mammalian cell surface polypeptide. Claims 16-17, which depend on claim 15, limit the mammalian cell surface polypeptide to mouse and human cell surface polypeptide, respectively. Claim 18, which depends on claim 1, limits the ligand for a cell surface polypeptide to a ligand for a cell surface polypeptide of a leukocyte, which is further limited to dendritic cells by claim 21. Claim 19, which depends on claim 1, limits the ligand for a cell surface polypeptide be a ligand for a cell surface polypeptide of an antigen presenting cell, which is further limited to a professional antigen presenting cell

by claim 20. Claims 22 and 24, which depend on claim 1, limit the ligand for a cell surface polypeptide to a ligand for a mouse GM-CSF receptor and to comprise a mouse GM-CSF receptor, respectively. Claims 25 and 27, which depend on claim 1, limit the ligand for a cell surface polypeptide to a ligand for a human GM-CSF receptor and to comprise a human GM-CSF receptor, respectively. Claim 69, which depends on claim 1, requires the fusion polypeptide to comprise a secretory signal sequence.

Babai et al. teaches a composition comprising two amino acid sequences. The first amino acid sequence is that of the influenza hemagglutinin. The second amino acid sequence is that of GM-CSF. The influenza hemagglutinin used by Babai et al. is derived from influenza A/Shangdong/9/93, which is H3N2 subtype that infects humans. Hemagglutinin (HA) is a lectin, which has a carbohydrate-binding domain. HA is also binds to sialic acid, as evidenced by Masuda et al. Masuda et al. also evidences that sialic acid derivatives include the following structures: N-acetylneuraminic acid, alpha-NeuNAc-[2->6]-Gal, alpha-NeuNAc-[2->6]-GalNAc and alpha-NeuNAc-[2->3]-Gal. In the instant case, Babai et al. used the entire HA protein, which comprises at least 10 contiguous amino acids and includes the HA1 portion. The GM-CSF used by Babai et al. is a ligand for a mammalian cell surface polypeptide, particularly that of mouse. Specifically, the ligand is a ligand for a cell surface polypeptide of a leukocyte, specifically dendritic cells, which is a professional antigen presenting cell. In the instant case, because Babai et al. used the entire GM-CSF sequence, Babai et al. used at least 5 contiguous amino acids of a the mouse GM-CSF.

The difference between the claimed invention and the invention is: Babai et al. did not fuse the two amino acid sequences. However, the deficiency noted in Babai et al. is fully compensated by Faulkner et al. Additionally, Faulkner et al. teaches a vector comprising a nucleic acid molecule encoding for the fusion polypeptide. The fusion polypeptide of Faulkner et al. comprises a secretory signal sequence.

Faulkner et al. teaches that the immunogenicity of a peptide vaccine may be improved by fusing antigen and cytokine. In the instant case, the HA used by Babai et al. is an antigen and GM-CSF is a cytokine. Hence, at the time the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to fuse the HA antigen of Babai et al. with GM-CMSF. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to improve the immunogenicity of the vaccine made by Babai et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because Faulkner et al. demonstrated fusion improved immunogenicity.

It would also been prima facie obvious for one of ordinary skill in the art to obtain the nucleic acid sequence of the fusion polypeptide rendered obvious by Faulkner et al. and Babai et al. One of ordinary skill in the art, at the time the invention was made would have been motivated to do so to express the fusion polypeptide rendered obvious by Babai et al. and Faulkner et al. One of ordinary skill in the art, at the time the invention was made would have had a reasonable expectation of success for doing so because the use of nucleic acid sequences to encode fusion polypeptides is routinely practiced in the art. See MPEP 2143.01, *Ex parte Kubin*.

While it is not readily apparent if Faulkner et al. fused the antigen to the N or C terminal of the cytokine, however, it is noted that there exist 2 fusion sites, either the N or the C terminal. Thus, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to fuse the HA antigen of Babai et al. to either the N or the C terminal of GM-CSF. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to fuse the antigen and cytokine. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because there are a finite number of fusion sites.

It is noted that some of the claims requires the use of a human GM-CSF. In the instant case, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to substitute the mouse GM-CSF used by Babai et al. to that of a human GM-CSF. One of ordinary skill in the art, at the invention was made, would have been motivated to do so to make a fusion composition that is suitable for human use. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution of known/functional alternatives is routinely practiced in the art.

Additionally, while the subtype used by Babai et al. is not an H1 subtype or is the A/PR/8/34; however, at the time the invention was made, this subtype and strain has been well characterized, as evidenced by the disclosure of Masuda et al. Thus, it would have been prima facie obvious for one of ordinary skill in the art, at the time the invention was made, to substitute the HA antigen of Babai et al. to that of the HA

antigen derived from A/PR/8/34 strain, which is an H1 subtype. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do so to make a composition that is specific for the particular A/PR/8/34 strain. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the substitution of known/functional alternatives is routinely practiced in the art.

5. Claims 1 and 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Babai et al. in view of Faulkner et al., as evidenced by Masuda et al., as applied to claim 1, in further view of Shao et al.[4]

Claim 67, which depends on claim 1, requires that a linker interposed between the first and second amino acid sequences. Claim 68, which depends on claim 67, requires the linker to be $(Gly_xSer)_n$, wherein n is between 1-15 and x is between 1-10.

The significance of Babai et al., Faulkner et al. and Masuda et al., as applied to claim 1 is provided above.

Babai et al., Faulkner et al. and Masuda et al. do not teach the use of a linker. However, Shao et al. teaches the use of a linker to minimize steric hinderance between two sequences. The linker used by Shao et al. is $(GlySer)_5$. Thus, at the time the invention was made, it would have been prima facie obvious for one of ordinary skill in the art to use $(GlySer)_5$ as a linker interposing between the HA antigen and GM-CSF of Babai et al. One of ordinary skill in the art, at the time the invention was made, would have been motivated to do to minimize any steric hinderance posed by linking HA with

GM-CSF. One of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success for doing so because the use of linkers is routinely practiced in the art.

Conclusion

6. No claims are allowed. As noted above, to allow the entry of the rejection(s) set herein, the office action is non-final.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571)272-0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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[4] Shao et al. Anchor-Chain Molecular System for Orientation Control in Enzyme Immobilization. Bioconjug., Chem., 2000, Vol. 11: 822-826.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Le/
Primary Examiner, Art Unit 1648

/E. L./